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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/445,963	12/16/1999	TOHRU TANAKA	Q57226	1604

7590 09/20/2004

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EXAMINER

YU, MISOOK

ART UNIT PAPER NUMBER

1642

DATE MAILED: 09/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

09/445,963

Applicant(s)

TANAKA ET AL.

Examiner

MISOOK YU, Ph.D.

Art Unit

1642

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 30 June 2004.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 10-46 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 10-15, 18-21, 28-43 and 46 is/are allowed.
- 6) ☒ Claim(s) 16, 17, 22, 24, 26, 27, 44 and 45 is/are rejected.
- 7) ☒ Claim(s) 23 and 25 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

Applicant's submission filed on 06/30/2004 is acknowledged. Claims 14-46 are new. Claims 10-46 are pending and under consideration.

This Office action contains new grounds of rejection.

#### ***Claim Rejections - 35 USC § 103, Withdrawn***

The rejection of the claims under 35 U.S.C. 103(a) as being unpatentable over Kennedy et al (1994, ACS Symp. Ser., pp.291-302) in view of Jichlinski, et al (1996, Pro. SPIE-Int. Soc. Opt. Eng. pp.340-347), Kajiwara (1990, JP 02111747), and Jaffe, et al (1990, Biochemistry, pp.8345-50) is withdrawn because applicant argument is persuasive.

#### ***The Following Are New Grounds of Rejection***

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16, 17, 22, 24, 26, 27, 44, and 45 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for art-known radioisotopes for art-known NMR techniques, does not reasonably provide enablement for nitrogen isotope N-13 for NMR or the diagnosis and treatment simultaneously being carried out. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use and make the invention commensurate in scope with these claims.

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The claims are drawn to method of cancer detection and treatment by administering carbon or nitrogen isotope labeled 5-ALA to patient, followed by detecting cancer using NMR, wherein the malignant tumor is detected with a higher sensitivity using NMR (claims 16, and 17), wherein  $^{13}\text{N}$  isotope is used (claims 22, and 24), wherein detection is by using a plurality of NMR (claims 26, and 27), wherein the detection and treatment are done at the same time (claims 44, and 45).

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The specification at pages 7, and 8 teaches that carbon or nitrogen isotope-replaced 5-aminolevulinic acid (5-ALA) higher measuring sensitivity than deuterium-replaced 5-ALA. The specification also teaches that carbon isotopes or  $^{15}\text{N}$  isotope could be incorporated to 5-ALA by various art-known methods.

In order to practice the claimed invention in the newly presented claims 22, and 24, one of skill has to know how to make and use  $^{13}\text{N}$  labeled 5-ALA. However, neither the specification nor any art of record teaches how to make and use  $^{13}\text{N}$  labeled 5-ALA in combination with NMR.

As for claims 16, and 17, the specification only teaches higher sensitivity as compared to deuterium labeled 5-ALA. The base claim 10, and 12 are not drawn to deuterium labeled 5-ALA. Newly presented claims 16, and 17 as currently drafted appear to suggest that there would be a higher sensitivity NMR as compared to the base claim 10, and 12. However, the specification does not teach what makes NMR results in a higher sensitivity as compared to the active step described in the base claims. One of skill would have to resort into undue experimentation to figure out what is required to make the active steps of the base claims in order to practice the claimed invention in the newly presented claim 16, and 17.

As for claims 26, and 27, the specification does not teach any new NMR techniques other than saying the carbon or nitrogen isotope labeled 5-ALA higher utilization energy.

Creighton, T (1993, Proteins, 2<sup>nd</sup> edition, W. H. Freeman and Company, NY, pages 238-243 only) teaches NMR spectra are generated by placing a subject of interest in a magnetic field and applying radio-frequency pulses, which perturb the equilibrium nuclear magnetization of those atoms with nuclei of nonzero spin.

Jaffe et al., of record at page 8346 under the heading "Experimental Procedures" teach that the spectra of <sup>13</sup>C-labeled 5-ALA is obtained by applying magnetic radio-frequency pulses at 75.45 MHz while the spectra <sup>15</sup>N-labeled 5-ALA is obtained by obtained by applying magnetic radio-frequency pulses at 60.8 MHz. It is not clear how a plurality of NMR could be accomplished when different frequencies of magnetic fields are necessary for different isotopes.

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As for claims 44, and 45, Merriam-Webster Online downloaded on 9/16/04 from [url>>www.m-w.com](http://www.m-w.com) defines "isotopes" as "any of two or more species of atoms of a chemical element with the same atomic number and nearly identical chemical behavior but with differing atomic mass or mass number and different physical properties." This indicates  $^{12}\text{C}$ ,  $^{13}\text{C}$  and  $^{14}\text{C}$  are all carbon isotopes. The specification at page 7 teaches that 5-ALA is made up of 5 carbon atoms and one nitrogen atom. It appears that a carbon isotope with nuclei of either nonzero spin or zero spin is necessary in order for 5-ALA molecule to be existed.

Considering the unpredictable state of art, limited guidance, no examples in the specification how to make and use the instantly claimed invention, it is concluded that undue experimentation is required to practice the full scope of the claimed invention.

#### ***Allowable Subject Matter***

Claims 10-15, 18-21, 28-43, and 46 allowed.

Claims 23, and 25 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

#### ***Conclusion***

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

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A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 571-272-0839. The examiner can normally be reached on 8 A.M. to 5:30 P.M., every other Friday off.

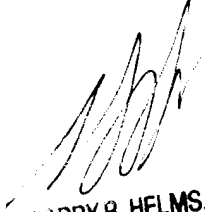
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey C Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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MISOOK YU, Ph.D.  
Examiner  
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LARRY R. HELMS, PH.D.  
PRIMARY EXAMINER